Intracranial Pressure (VIIP) syndrome is likely related to a head-spinal fluid pressure after returning to Earth. This Visual Impairment with optic disc edema showed moderate elevations of cerebral vision impairment. In addition, lumbar punctures in four astronauts six-month missions to International Space Station show unexpected. Recent ophthalmic evaluations of seven astronauts after. 24-h monitoring of intraocular pressure (IOP) patterns can be. Purpose: Twenty-five normal healthy non-smoking volunteers participated in this study (mean age: 31 years). Right and left IOP, ICP (non-invasive ultrasound pulsed phase locked loop), arm blood pressure, and heart rate were measured during the last minute of each testing condition. Subjects were positioned supine (5 mins), sitting (5 mins), 15-degrees head-down tilt (HDT) (5 mins) and ten minutes of HDT with LBNP (25 mmHg). The order of HDT and HDT+LBNP tests were balanced. The right and left IOP values were averaged and used for statistical analysis (significance accepted at p<0.05). Data are presented as mean ± standard deviation. The change from supine was calculated for IOP values. Results: IOP significantly decreased from supine to sitting posture by 3.2 ± 1.4 mmHg, and increased by 0.9 ± 1.3 mmHg from supine to the HDT position. LBNP during head-down-tilt significantly lowered IOP to supine levels (difference from supine, 0.3 ± 1.1 mmHg). In addition, added LBNP during HDT significantly decreased ICP-related pulse amplitudes of transcranial ultrasound waveforms by 2.1±3.4 microns (n=9). Mean blood pressure and heart rate did not change significantly across all conditions. Conclusions: These data demonstrate that short duration exposures to HDT increase IOP and ICP significantly and further, that LBNP counteracts these elevations of IOP and ICP. Therefore, spaceflight countermeasures that shift fluid to lower body may mitigate vision problems. Commercial Relationships: Brandon R. Macias, None; Noelia Grande Gutiérrez, None; Alan Hargens, None; John H. Liu, None Support: BRM supported by NSBRI postdoctoral fellowship, NGG supported by the la Caixa foundation fellowship, and study funded by NASA grant NNX13AJ12G (to ARH).

Assessment of sleep stages and relationship to intraocular pressure patterns using a contact lens sensor
Kaweh Mansouri, Tarek Shaarawy: Glaucoma sector, Division of Ophthalmology, University of Geneva, Geneva, Switzerland. Purpose: To evaluate whether information from a contact lens sensor for 24-h monitoring of intraocular pressure (IOP) patterns can be used to distinguish sleep stages. We further hypothesized that IOP patterns may be higher in the rapid eye movement (REM) phase. Methods: 12 healthy subjects underwent simultaneous ambulatory 24-h monitoring of IOP patterns using a contact lens sensor (CLS; Triggerfish, Sensimed AG, Switzerland) and sleep monitoring using a validated wireless system (WS; ZEO, Newton, MA, USA) that collects electrophysiological signals from the forehead with a single bi-polar channel. The CLS measures ocular dimensional changes at the corneo-scleral junction that are assumed to be related to IOP changes. The WS distinguishes 4 sleep stages: wake, light sleep, deep sleep, REM. Intraclass correlation coefficients (ICC) were calculated for comparison of CLS and WS-derived sleep stages. Results: Data on both IOP and sleep stages could be obtained in 10 subjects (mean age 42 ± 10.2 years; 60% women). Four different patterns of CLS-data could be distinguished during sleep: high-frequency sinusoidal pattern, low-frequency sinusoidal pattern, and irregular pattern. The irregular pattern correlated well with the WS-derived REM stage (ICC=0.91), while the other two CLS stages did not correlate well with WS sleep stages (ICC=0.47). IOP patterns during CLS-derived REM stages were higher than during non-REM sleep stages (128 ± 52 mV vs. 108 ± 42; p=0.044). Conclusions: Results show a good agreement between CLS and WS recordings of REM sleep. This work further supports a possible use of combined sleep and IOP pattern monitoring in glaucoma patients. Commercial Relationships: Kaweh Mansouri, SENSIMEDE AG (C); Tarek Shaarawy, None Support: SENSIMEDE AG, SWITZERLAND

Single Versus Multiple Intraocular Pressure Measurements in Glaucoma Surgical Trials
Mingjuan L. Zhang, Brian Chow, Jiangxia Wang, Gerard Smits, Shan C. Lin, Tsonito Ianchulev, Henry D. Jampelet. Johns Hopkins University School of Medicine, Baltimore, MD; Duke University, Durham, NC; Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; Transcend Medical, Menlo Park, CA; University of California, San Francisco, San Francisco, CA; Wilmer Eye Institute, Baltimore, MD. Purpose: Little is known about the necessity of multiple same-day intraocular pressure (IOP) measurements versus a single measurement in describing the effect of IOP-lowering surgical procedures, and such evidence could affect surgical trial recruitment and retention. Methods: 609 patients (609 eyes) with primary open-angle glaucoma and cataract from the pre-randomization phase of the COMPASS CyPass Micro-Stent randomized controlled trial underwent one IOP measurement while taking usual medications to lower IOP and three diurnal IOP measurements at 8am, 12pm, and 4pm after undergoing a 2-4 week washout of all IOP-lowering drops. The main outcome was the proportion of eyes in which the increase in IOP after washout, using the mean of the three measurements, differed by more than 0, 1, 2, or 3mmHg from the increase in IOP after washout using only one of the after-washout measurements. A proportion of ≥10% at the 1.5mmHg cutoff was considered clinically acceptable. Results: The mean IOP before washout was 18.5±4.0mmHg. The mean increase in IOP after washout using the mean of the three measurements was 5.3±4.2mmHg. The percentage of eyes in which the increase in IOP using a single after-washout IOP differed from the increase in IOP using the mean of three measurements by more than 1.5 mmHg was 3%, 26%, 34%, 30%, and 31% when the single measurement was made at 8am, 12pm, 4pm, a randomly chosen one of the three times, and the time closest to that of the before-washout...
IOP, respectively. By logistic regression, the 12pm after-washout IOP had the lowest proportion of eyes differing from the mean (p<0.001) and thus most closely approximated the mean diurnal IOP measurement.

**Conclusions:** Although eliminating multiple IOP measurements would simplify the conduct of surgical trials in glaucoma, our data show that using a single IOP measurement after washout does not adequately approximate the mean of multiple IOP measurements. Further evaluation is needed after the COMPASS trial is complete to determine whether single IOP measurements might have applicability for post-surgical IOP characterization.

**Commercial Relationships:** Mingjuan L. Zhang, None; Brian Chon, Transcend Medical (F); Jiangxia Wang, None; Gerard Smits, Transcend Medical (C); Shan C. Lin, None; Tsontcho Ianchulev, Transcend Medical (E); Henry D. Jampel, Transcend Medical (C)

**Clinical Trial:** NCT01085357

**Program Number:** 2167
**Presentation Time:** 4:30 PM–4:45 PM

**Nanophotonics-based Intraocular Pressure (IOP) Sensor with Remote Optical Readout**

Kun Huang¹, Jeong O. Lee², Christopher F. Divsalar², Trong T. Nguyen², David W. Sretavan², Hyuck Choo¹. ¹Electrical Engineering, California Institute of Technology, Pasadena, CA; ²Ophthalmology & Physiology, University of California, San Francisco, San Francisco, CA.

**Purpose:** To develop a miniaturized nanophotonics-based implantable device for frequent, automated remote monitoring of IOP.

**Methods:** The basic nanophotonics IOP sensor consists of a sealed cylindrical chamber, with gold nanodot arrays on flexible membranes forming the top & bottom chamber surfaces (Fig. 1 A). When interrogated with light, the reflected signal from the device shows maximal reflectance dips at specific wavelengths, and is the spectral signature of a unique gap size between nanodot arrays. Within the anterior chamber, the nanodot membranes deform as the ambient pressure, i.e. IOP rises, causing the gap between arrays to decrease (Fig. 1 B). This gap narrowing causes the reflectance spectrum to shift (Fig. 1 C, D), and is detected remotely via a spectrometer.

**Results:** Proof of concept devices were fabricated consisting of two thin rigid glass substrates containing gold nanodot arrays, separated from each other by ~6 μm-thick photoresist (Fig. 2 A). 5 devices with gaps of 6.32, 6.38, 6.45, 6.51, and 6.60 μm were interrogated and the reflected signal analyzed using a spectrometer. The reflectance spectra showed a systematic shift in the reflectance dip maxima with increasing gap separation (Fig. 2 B), in agreement with predictions from simulation. Prototypes were also implanted into rabbit eyes ex vivo (Fig. 2 C, D). A reflectance spectrum with identifiable reflectance dips was detected remotely at 7 mm from the nanodot arrays (Fig. 2 F).

**Conclusions:** A nanophotonics-based method of IOP sensing is in principle viable. Advantages of this approach include potential miniaturization to obtain 25-50 μm devices and remote sensing using light ultimately at a distance of 5 cm or larger.
Fig 2. A) Schematic of rigid coverslip prototypes with nanodot arrays. B) As the gap size decreases, the resonance systematically shifted to a shorter wavelength. C) Nanophotonics sensor in rabbit anterior chamber. D) Higher mag. Arrow shows 50 X 50 μm² sensor array. Scale = 1 mm. E) Reflectance spectrum from sensor in saline. Arrows show reflectance dips. F) Spectrum from same sensor in anterior chamber.

Commercial Relationships: Kun Huang, None; Jeong O. Lee, None; Christopher F. Divsalar, None; Trong T. Nguyen, None; David W. Sretavan, None; Hyuck Choo, None

Support: Caltech Innovation Fund & Barroths Wellcome Fund

Program Number: 2168
Presentation Time: 4:45 PM–5:00 PM
Development of an implantable system for controlling intraocular pressure in rats
Simon Bello¹, Sharad Malavade², Christopher L. Passaglia¹,²
¹Chemical and Biomedical Engineering, University of South Florida, Tampa, FL; ²Ophthalmology, University of South Florida, Tampa, FL.

Purpose: To devise a system for continuously recording and regulating intraocular pressure in a rat’s eye in order to induce ocular hypertension and monitor IOP fluctuations on a 24-hour basis.

Methods: The system consists of a pressure sensor, a controller, and a fluid micropump; these elements interact with the rat’s eye via a special cannula implanted in the anterior chamber. The tubing, filled with artificial aqueous humor, is tunnelled subcutaneously from an incision in the scalp to the orbit of the eye. A novel surgical procedure was developed to penetrate the cornea and hold the cannula in place without damaging internal ocular structures, even though the eye moves. The cannula directly conducts pressure from inside the eye to the pressure sensor. IOP signals were then sent to a data acquisition board for analysis and display. The system was tested by exposing it to constant hydrostatic pressure for weeks on end. It was also used on rats under ketamine anesthesia to record natural IOP fluctuations for 12–48 hours and to hold IOP at set levels of 10–50 mmHg for several hours each.

Results: The system successfully recorded long term data with a resolution of 0.2 mmHg, noise oscillations of less than 1 mmHg, and no drift under constant hydrostatic pressure. When the system was connected to anesthetized rats, circadian rhythms in IOP with fluctuations of up to 10 mmHg were recorded. When the system set point was changed, IOP was raised or lowered to the specified pressure level in a few seconds and then maintained within ±3 mmHg of that level. Little-to-no sign of physical or physiological damage was evident to the rat’s eye after months of cannula implantation.

Conclusions: Results show that cannulation of the anterior chamber of a rat’s eye is possible and its combination with a dynamic feedback system allows researchers to continuously record and regulate IOP for long periods of time, paving the way towards an implantable IOP control system for rats and larger animals.

Commercial Relationships: Simon Bello, None; Sharad Malavade, None; Christopher L. Passaglia, None

Program Number: 2169
Presentation Time: 5:00 PM–5:15 PM
Pulse-dependent Trabecular Meshwork Motion: Direct Microscope Observation and Measurement in Radial Limbal Segments of Non-human Primate Eyes
Murray A. Johnstone, Elizabeth Martin, Yi Jiang. Ophthalmology, University of Washington, Seattle, WA.

Purpose: To describe a microscopic technique to observe, video & measure large pulse-dependent trabecular meshwork (TM) excursions into Schlemm’s canal (SC) and associated recoil that occur on a time scale of milliseconds.

Methods: Measurement of pulse-induced TM motion in radial segments in ex vivo macaca nemestrina eyes (5), radial 350 um limbal segments (10), cornea and sclera of segments pinned into paraffin in Petrie dish, ciliary body tensioned under direct visualization to optimize SC dilation, then pinned; 45-power microscope. Syringe attached to 27 gauge cannula (ID 200 um), 18 mpixel camera, videography (30 fps), micrometer. FIJI image analysis program for measurement of Schlemm’s canal anterior-posterior (AP) length, SC height (SCH), SC area (SCA) & length of apposition between SC inner and SC external wall (SCAP).
intervals were from baseline until no further TM distention or recoil could be detected.

Results: Videography demonstrated easily visible pulse-dependent TM movement in response to pulse waves in each of the radial segments. Analysis of a pulse wave (Fig. 1 & 2) involved TM movement duration of 167 msec.; SCH decreased from 85 to 16 um, (TM velocity 390 um/sec); SCA decreased from 12,823 to 452 um$^2$; SCAP increased from 0 to 166 um progressing from anterior to posterior along SC length, reducing linear area of open SC from 226 to a 44 um region at a V-shaped area of a collector channel ostia at the posterior end of SC. In another segment, TM elasticity was assessed by measuring SCH to determine distension and recoil in 5 infusion cycles. Distention duration mean 586±219 msec. Velocity 23.4±12.5 msec. Recoil duration mean 526±132 msec. Velocity 17±6.4 msec.

Conclusions: The microscope technique permits direct observation, videography and measurement of TM motion. Observable and measureable characteristics of TM movement include distention and recoil involving SCH, SCA, SCAP and velocities. The TM appears to be markedly compliant with elastic properties making it capable of undergoing rapid large excursions into SC in response to IOP transients. Such excursions may induce rapid SC volume changes in vivo.

Fig. 1 Trabecular meshwork and Schlemm’s canal appearance before an after an infusion pulse wave.
Stiffness of the Trabecular Meshwork In Living Eyes

Larry Kagemann1, 2, Mark Johnson3, Bo Wang1, 2, Gadi Wollstein1, Hiroshi Ishikawa1, 2, Zach Nadler1, Ian A. Sigal1, 2, Yun Ling1, 4, Richard A. Bilouk1, 4, Joel S. Schuman1, 2. 1UPMC Eye Center, Eye and Ear Institute, Ophthalmology and Visual Science Research Center, Department of Ophthalmology, University of Pittsburgh, Pittsburgh, PA; 2Department of Bioengineering, Swanson School of Engineering, University of Pittsburgh, Pittsburgh, PA; 3Departments of Biomedical Engineering, Mechanical Engineering and Ophthalmology, Northwestern University, Evanston, IL; 4Department of Biostatistics, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA.

Purpose: Trabecular meshwork (TM) stiffness has been shown to be elevated in cadaveric glaucomatous eyes (mean 80.8, range 0.5-565 kPa) compared with normal eyes (4.0, 0.5-10kPa) [Last et al, IOVS 2011(52):5:2147-2152]. However; those measurements were made in isolated tissues by atomic force microscopy. In-vivo, the TM is suspended in tension between the posterior cornea and ciliary body. Ciliary muscle activity may increase the effective stiffness of the TM. We examined this hypothesis in living eyes, comparing the effect of IOP on outflow pathway morphology with previous measurements made in cadaveric eyes.

Methods: The temporal limbus of 33 eyes of 19 healthy subjects (12 male, 7 female, age 40 ± 15 years) was imaged by spectral-domain optical coherence tomography (Cirrus HD-OCT, Zeiss, USA) at baseline and during IOP elevation (ophthalmodynamometer applied at 30 Grms force). IOP was measured at baseline and during IOP elevation by Goldmann applanation tonometry. Vascular landmarks were used to identify corresponding locations in baseline and IOP elevation scan volumes. Schlemm’s canal cross-sectional area (SC-CSA), mean inner to outer wall distance (IOD) and mean TM thickness (TMt), the distance from the anterior chamber to SC inner wall, were measured at 5 locations within a 1 mm length of SC using ImageJ as described previously [IOVS 2010; 51(8): 4054-4059]. Data were compared with measurements by VanBuskirk et al in cadaveric eyes (IOVS, 1982;22(5):625-32, Table).

Results: A mean increase in IOP of 23 mmHg (Table) led to a decrease of SC-CSA (39%) and IOD (18%) while TMt was not unchanged (Table). In cadaveric eyes, the decreases in SC-CSA were greater than in live eyes (Table), but the TMt was also insensitive to IOP elevation.

Conclusions: The collapse of Schlemm’s canal with increasing IOP while TM thickness changed little suggests that the TM acts as a membrane under tension. This was true both in live and cadaveric eyes. However, the 39% decrease in SC-CSA and IOD with increasing IOP in living eyes, was smaller than the decrease observed in cadaveric eyes. This suggests that the tension and thus, the effective stiffness of this membrane may be greater in live eyes, presumably due to ciliary muscle contraction. The contribution of the TM in preventing collapse of the SC may differ in living versus cadaveric eyes.

Program Number: 2170
Presentation Time: 5:15 PM–5:30 PM

Commercial Relationships:
Murray A. Johnstone, Alcon (C), Allergan (P), Cascade Ophthalmics (C), Healionics (C), Ivantis (C), University of Washington C4C (P); Elizabeth Martin, None; Yi Jiang, None

Fig. 2 Measurements from images in Fig. 1

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